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Hereditary Resistance to Disease

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Selective breeding as a method of disease control

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AT THE present time effective suppression of infectious animal diseases is obtained by a combination of control measures, which consist largely of sanitary procedures, eradication of carriers, and of attempts to fight the infection by aiding the animal's natural resistance by augmenting or exciting the body defenses. These aids consist of biologics which are of immense value in preventing and arresting the progress of disease, the use of drugs and antibiotics which are highly useful in halting some disease processes, and selective breeding which could prevent or reduce the severity of incipient infections. Genetics is the last of the 3 means of combating infectious animal diseases to be used consciously toward that end.

Role of Genetics

Predisposing factors for or against disease have been recognized from the earliest times as being inheritable. However, the use of the science, genetics, for breeding animals capable of resisting an infectious agent, or more able to combat infection which has started, has had to await the discovery and application of the laws which govern it. These laws are, after all, the unchanging facts of genetics and they could not be applied to disease until they were relatively well understood. Once these facts were established the possibility of founding resistant lines in each species and spreading them throughout the breeds came a step nearer to practical use.

Fighting animal disease is a proposition of finding the most successful method of conquering any enzoötic or epizoötic condition and using that method wherever it is suitable. For purposes of lowering the incidence of diseases, immunizing substances, eradication, and genetics each has a part to fulfill, and without prejudice we must examine the results obtained by each and assign to it the value and consequent use due it. The veterinarian's duty as an advocate of disease control is to be aware of the progress made by animal husbandrymen, pathologists, and geneticists, and to use the most advanced methods that have proved successful.

Plant pathologists are far ahead of animal breeders in producing resistant stock because other methods of combating diseases are less successful economically with plants. Considering their small individual worth and widespread cultivation, it is too expensive to treat plants. But for the plant breeder, this cheapness, short generation time, and large numbers of progeny per plant constitute ideal material with which to work. The accomplishments of plant breeders in producing resistant or immune varieties have provided knowledge of methods and possible goals which probably will help show the way to the man working with animals.

The problem of genetic resistance to disease is not one which is easily solved. A primary problem is that of obtaining the resistant stock. Occasionally a small group of animals is found which is resistant to a disease, either being refractory to it, or suffering only mildly with a rapid and complete recovery. An example is

Algerian sheep which are not susceptible to anthrax. These instances afford an opportunity for the geneticist to attempt to isolate them in pure lines, discover the cause of the resistance and the mode of inheritance, and to develop enough of the resistant animals that their influence may be spread throughout the breed. On one occasion in Iowa, a boar and 9 sows that were refractory to hog cholera were used in an attempt to breed a line of hogs resistant to that disease[1]. Each year a few would survive the virus inoculations, but the experiment ended for lack of funds with the conclusion that the results obtained over 4 years certainly indicated that simple selection is not directly effective in increasing cholera resistance.

Selective Breeding

An experiment was conducted by Roberts and Card of the Illinois Agricultural Experiment Station[2] for several years trying to breed for hog cholera resistance. Animals that appeared to be naturally resistant were used as breeding stock and their offspring tested for resistance to the disease by exposure to it. It was intended that if resistance were hereditary, an attempt would be made to discover the mode of inheritance and to establish resistant strains. For several years 3 resistant animals were found each year, but in 1936 all of the offspring died. The experimenters decided that before going further they must learn more about immunology and about what methods would work best. That knowledge could be more cheaply gained on smaller laboratory animals. Since then, most of the experiments on breeding for disease resistance in animals have been conducted on mice, rats, and chickens.

Another tack in establishing genetic resistance is to decide what disease or diseases the animal shall be resistant to and proceed deliberately to build that resistance by means of a process of infection and survival on a basis of family selection. Lambert, who had done the Iowa State hog cholera investigation, began an experiment with a highly susceptible flock of White Leghorns. In 6 years mortalities from fowl typhoid, *Shigella gallinarum,* were reduced to about 10 per cent in the lines selected for resistance as against something over 85 per cent in the lines with which he started.[3] Roberts and Card, of the Illinois experiment mentioned, began an intensive study of pullorum disease accompanied by a selective breeding program.[4] One of their aims was to demonstrate that there were intra-specific differences in disease resistance. They proved that resistance and susceptibility in the chicken to infection by *Salmonella pullorum* were hereditary. Their selection was effective in producing strains more resistant than the unselected stock, which maintained the resistance through successive generations and which transmitted resistance when crossed with susceptible stock. These and similar experiments including the development of mice resistant to mouse typhoid, and the discovery of natural cases in which breeds differed in susceptibility to an organism opened the new field. The investigations indicated that it is best to use inbred lines because only with fairly uniform lines can accurate diagnoses be made. It was also established that family selection was necessary to create lines of resistant stock. These could then be multiplied to give numbers. This necessitates culling by large numbers which is difficult to do, especially with the larger farm animals, while maintaining sufficient subjects for the tests.

Poultry Diseases

These breeding results stimulated research into the adjoining field of genetics because it was necessary to know the complexity and pattern of inheritance in order to increase the resistance and transmit it. Inquiry into the disease pathology was instituted from a desire to know the causes of heritable resistance (whether due to anatomical resistance, or the serological attributes of the blood) so that it might be duplicated. In pullorum disease it was found to be related to the number of lymphocytes which is greater in resistant than in susceptible chicks. The lymphocyte count and resistance increase with the chicks' age, but if the number of lymphocytes is reduced by use of the X-ray, susceptibility increases. In the resistant chick the number of lymphocytes is high at the time of normal greatest incidence of the disease, which is usually within the first week after hatching.

In experiments on resistance to neoplasms it was found that the number of erythrocytes and leucocytes was fixed with the latter quite high. The proportions of the leucocytes varied, indicating that breeding may fix the number of the parent cells, but that differentiation into types is dependent on interactions of the body and its environment. This has a bearing on the resistance.

These instructive preliminaries, though they are still being continued, have been used as a basis for practical flock experiments in a number of cases. Cornell, Pennsylvania, New Jersey, and California have all endeavored to reduce total flock mortality. Since 1930 there has been an increased mortality among older chickens due largely to the "fowl leucosis complex." At the same time chick mortality had decreased, due largely to better control of pullorum disease. In avian lymphomatosis, the diseased stock may be culled fairly easily because of the symptoms which are paralysis of the wing or leg, blindness, deformed or gray pupils, and tumors of the skin and internal organs which may all be manifestations of the same complex.

Viable Families

At the Pennsylvania Agricultural Experiment Station[5], the selection is on a family basis with all deaths and culling for poor health charged as mortality. During one of the first years of the experiment, there was a high mortality due to range paralysis in which the progeny of some birds lived satisfactorily while heavy or complete losses occurred among the offspring of others. Over a period of 5 years the laying flock mortality went down 50 per cent; there was an increased laying flock viability but the chick mortality increased slightly. A viable family was designated as one with 5 full sisters living throughout the laying year. Viable families were developed and their blood was spread throughout the flock. "The increase in viability was accomplished by the development of families which possessed greater resistance to disease." That it was not merely greater general constitutional vigor is proved by the slightly increased chick mortality and the constant hatching percentage. At New Jersey[6] in lines selected for resistance to range paralysis, the incidence of the disease went from 33.0 per cent to 3.5 per cent infected. The percentage of laying house mortality went down also. Virtually the same results were obtained in the other flocks.

Practical Application

The field of work on genetic resistance has moved back into large animals again. At the University of California, a herd of swine has been bred that is absolutely refractory to brucellosis. It is encouraging that the offspring are equally resistant to date. Another large animal experiment at the California station concerns the variation in resistance and susceptibility to sheep stomach worms, *Ostertagia circumcincta,* among Romney Marsh sheep. There are variations in fecal egg counts from animals under identical conditions that can only be attributed to inherited differences in susceptility. The progeny of some rams tend to resistance while those of others tend to susceptibility.

Is all of this leading to anything practical? The Cornell investigators claim to have demonstrated that it is feasible to breed for resistance to disease and at the same time improve the flock with respect to other economically important qualities. In their flock while cutting mortality from 64 per cent to 38 per cent on a 500 day basis they increased (a) the size of the birds, (b) the size of their eggs, and (c) their ability to lay. There was a remarkable reduction in mortality in some of the Cornell flock that was outcrossed to a resistant flock linebred for viability. This gives some grounds for hoping that the introduction of such males in flocks not specifically bred for viability may prove an effective means of lowering mortality. The fact that individual males or

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The clinical picture is characteristic and diagnostic. It will be ascertained that an apparently normal pig will walk up to the food trough and partake of a mouthful or two of the food and shortly and suddenly thereafter it will display the seizure. This is marked by drawing the head backward, elevating the snout with the nostrils distended and the mouth open. The eyeballs are rolled backward, the legs become stiffened, and the animal falls to the ground. The thorax is expanded and the respirations are shallow and jerky. A distressing squeal is emitted. Profound coma ensues. This paroxysm lasts for only a few minutes but the patient usually remains recumbent for 5 to 15 minutes showing much evidence of exhaustion. At the expiration of this phase it will rise to its feet, advance to the trough again, and partake of the food without showing the least signs of discomfort. As a rule, a repetition of the seizure will occur at the next feeding period, especially if the interval between feedings is at least 3 or 4 hours. This will occur many times in some pigs and finally subside. Some pigs succumb, but the number that die from this condition is small. The age of the pigs involved ranges between 4 and 10 weeks.

Treatment

From the standpoint of the treatment and management of the epileptiform complex, one keeps in mind that he is dealing with a sporadic problem. Careful inquiry and inspection of the foodstuffs the affected pigs are receiving is imperative. It is also important to learn what foodstuff the mother of the patients received prior to the time the first case was noticed. This may extend into the period of gestation. We would especially call attention to cow's milk, because as stated above, our experience points to this foodstuff as the chief causative factor. This being the case, then it becomes apparent that the cow's milk should be the first foodstuff to withhold from the diet. When satisfactorily demonstrated that the disease continues after the cow's milk is removed from the diet, then it is necessary to hold back some other protein food. By trial and error in the process of elimination one should be able to establish with considerable certainty the responsible food factor or factors.

Immediate Treatment

Where immediate treatment of a suffering patient is the objective, then an intramuscular injection of adrenalin is advised. The dose of adrenalin for a 30 to 35 pound pig is 0.1 cc. of a 1:1000 solution. This will relax the muscles of the bronchioles and resuscitate a heart that fails to beat. The injection can be made directly into the heart muscle in case of heart failure but the dose must be decreased 30 per cent and the rate of injection reduced.

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females with unusually viable offspring are being produced suggests that further progress in increased viability is possible by using proved blood lines repeatedly.

Admittedly, there are difficulties hard to overcome. In building a new line of hardy stock entire families must be eliminated, so it may be beyond the means of an ordinary breeder. Transmission of the viability in repeated generations of the same blood line is necessary before one can be positive that he has a family that will survive an infection of any particular disease. Also, when this is established, there is no indication that the family will be resistant to any other disease since genetic resistance is probably specific for each disease. Further, the resistance is difficult to fix. It may often be lost in the first cross, and it is difficult to maintain a line of the improved stock.

Because of the variations in disease resistance within a species or breed, it seems entirely reasonable that the more resistant types may be selected naturally to some extent, provided exposure to infection is nearly universal. But such mass selection is much less effective than quantity selection for characteristics where the fate of the individual is much affected by things other than heredity. The selection of poultry breeding stock for family viability without a significant loss in the producing capacities of these birds gives ample reason for optimism, especially since present experiments show that the most viable birds are actually the highest producers. This gives more surviving birds to cull for other characteristics on which the financial state of the owner may more directly depend. Purebred Hereford cattle have a tendency toward cancer eye, so why not breed it out? That this is a possibility is shown by the Zebus which are resistant to it. Zebus are also but slightly affected by Texas fever, and it is thought that the Santa Gertrudis breed, whose ancestry is about ⅜ Zebu, is resistant in some degree. The same has been reported for damage done to these cattle by warbles and flies. Does this not point to fixing of resistant qualities and their subsequent spread through our livestock?

Currently the challenge is whether animal husbandrymen, pathologists, geneticists, and veterinarians can adapt their expanding knowledge of the field into a fertile source of disease resistant stock. This challenge is being met because it is the ambition of all of them to gradually eliminate disease or at least limit it as one of the vicissitudes of livestock raising. Genetic resistance is the final resort for those diseases that cannot be controlled through the cheaper means of vaccination and sanitation. When one of these 2 methods becomes established in controlling any disease, breeding against it usually will cease to be profitable.

Role of Veterinarian

If this field of activity becomes widespread there will be increasing need for more veterinarians to help with the diagnosis, with seeing that the test animals get a uniform exposure, and (if they ground themselves well enough in genetics) with summarizing and appraising the differences between families in disease resistance so that the actual selection and culling of families may be most effective. Provided that it can be done, this seems one of the most logical and practicable of the means available to proceed with eradicating disease and ridding ourselves of the recurrent annual cost of heavy livestock losses. The veterinarian must be cognizant of its value in controlling these plagues because it is now entering the realm of the practical.

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CURRICULUM

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in infectious diseases, Veterinary Hygiene 421, 422, and 423, will cover all 3 quarters, replacing the old courses, Infectious Diseases 421, Immunology 429, and General Hygiene and Epidemiology 422. It is considered more effective to cover all these subjects in relation to a single disease rather than to do it piecemeal in different quarters as heretofore. Veterinary Obstetrics 444 will be outlined to comprise a study of both infectious and non-infectious diseases of the generative organs of domestic animals, including related endocrine disturbances which impair reproduction. Special consideration will also be given to diseases of the newborn and the practice of artificial insemination. A new course in advanced animal nutrition, Animal Husbandry 518, is now required in the senior year. This course